UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 21, 2024

Zymeworks Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-41535**	**88-3099146**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

108 Patriot Drive, Suite A **Middletown, Delaware**	**19709**
(Address of principal executive offices)	**(Zip Code)**

(302) 274-8744
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	ZYME	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On November 21, 2024, Zymeworks Inc. ("Company") issued a press release announcing, with Jazz Pharmaceuticals plc, that the U.S. Food and Drug Administration ("FDA") has granted accelerated approval of Ziihera® (zanidatamab-hrii) for the treatment of adults with previously-treated, unresectable or metastatic HER2-positive biliary tract cancer ("BTC"). A copy of this press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information provided under this Item 7.01 (including Exhibit 99.1 attached hereto) is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

Zymeworks BC Inc. ("Zymeworks"), a subsidiary of the Company, is a party to an Amended and Restated License and Collaboration Agreement (as amended, the "License and Collaboration Agreement") with Jazz Pharmaceuticals Ireland Limited, a subsidiary of Jazz Pharmaceuticals plc, collectively referred to as "Jazz," granting Jazz exclusive rights to develop and commercialize Zymeworks' proprietary bispecific HER2 antibody product candidate known as zanidatamab throughout the world, but excluding certain territories already covered by Zymeworks' agreement with BeiGene, Ltd.

As announced on November 21, 2024, the FDA granted accelerated approval of Ziihera® (zanidatamab-hrii, a bispecific HER2-directed antibody that binds to two extracellular sites on HER2) 50mg/mL for injection for intravenous use for the treatment of adults with previously-treated, unresectable or metastatic HER2-positive BTC, as detected by an FDA-approved test. Ziihera® was approved under accelerated approval based on a 52% objective response rate and a median duration of response of 14.9 months as determined by independent central review from the HERIZON-BTC-01 trial, which included the evaluation of zanidatamab as a single agent in previously treated HER2-positive BTC. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the ongoing Phase 3 HERIZON-BTC-302 confirmatory trial, evaluating zanidatamab in combination with standard-of-care therapy versus standard-of-care therapy alone in the first-line setting for patients with HER2-positive BTC. Zanidatamab is also being investigated in a number of additional tumor types, including Phase 3 trials in gastroesophageal adenocarcinomas and metastatic breast cancer. This approval represents the first FDA-approved therapy in the Company's pipeline and offers the first and only dual HER2-targeted bispecific antibody and chemotherapy-free treatment for patients living with BTC.

Pursuant to the terms of the License and Collaboration Agreement, Zymeworks has earned a milestone payment of $25 million based on the FDA approval in BTC. Zymeworks remains eligible to receive up to $500 million in regulatory milestone payments and $862.5 million in commercial milestone payments, as well as tiered royalties of 10% to 20% of net sales by Jazz. For additional information regarding the License and Collaboration Agreement, please refer to the Company's Current Reports on Form 8-K, filed with the U.S. Securities and Exchange Commission on October 19, 2022 and on May 16, 2023.

Important Safety Information for Ziihera®

WARNING: EMBRYO-FETAL TOXICITY
Exposure to ZIIHERA during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.

- **Embryo-Fetal Toxicity**. ZIIHERA can cause fetal harm when administered to a pregnant woman. In literature reports, use of a HER2-directed antibody during pregnancy resulted in cases of oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death. Verify the pregnancy status of females of reproductive potential prior to the initiation of ZIIHERA. Advise pregnant women and females of reproductive potential that exposure to ZIIHERA during pregnancy or within 4 months prior to conception can result in fetal harm. Advise females of reproductive potential to use effective contraception during treatment with ZIIHERA and for 4 months following the last dose of ZIIHERA.
- **Left Ventricular Dysfunction**. ZIIHERA can cause decreases in left ventricular ejection fraction ("LVEF"). LVEF declined by >10% and decreased to <50% in 4.3% of 233 patients. Left ventricular dysfunction ("LVD") leading to permanent discontinuation of ZIIHERA was reported in 0.9% of patients. The median time to first occurrence of LVD was 5.6 months (range: 1.6 to 18.7). LVD resolved in 70% of patients. Assess LVEF prior to initiation of ZIIHERA and at regular intervals during treatment. Withhold dose or permanently discontinue ZIIHERA based on severity of adverse reactions. The safety of ZIIHERA has not been established in patients with a baseline ejection fraction that is below 50%.

- **Infusion-Related Reactions**. ZIIHERA can cause infusion-related reactions ("IRRs"). An IRR was reported in 31% of 233 patients treated with ZIIHERA as a single agent in clinical studies, including Grade 3 (0.4%), and Grade 2 (25%). IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.4% of patients. IRRs occurred on the first day of dosing in 28% of patients; 97% of IRRs resolved within one day. Prior to each dose of ZIIHERA, administer premedications to prevent potential IRRs. Monitor patients for signs and symptoms of IRR during ZIIHERA administration and as clinically indicated after completion of infusion. Have medications and emergency equipment to treat IRRs available for immediate use. If an IRR occurs, slow, or stop the infusion, and administer appropriate medical management. Monitor patients until complete resolution of signs and symptoms before resuming. Permanently discontinue ZIIHERA in patients with recurrent severe or life-threatening IRRs.
- **Diarrhea**. ZIIHERA can cause severe diarrhea. Diarrhea was reported in 48% of 233 patients treated in clinical studies, including Grade 3 (6%) and Grade 2 (17%). If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Withhold or permanently discontinue ZIIHERA based on severity.

Adverse Reactions

- Serious adverse reactions occurred in 53% of 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA.
- Serious adverse reactions in >2% of patients included biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhea (3.8%), gastric obstruction (3.8%), and fatigue (2.5%). A fatal adverse reaction of hepatic failure occurred in one patient who received ZIIHERA.
- The most common adverse reactions in 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA (≥20%) were diarrhea (50%), infusion-related reaction (35%), abdominal pain (29%), and fatigue (24%).

Use in Specific Populations

- **Pediatric Use**. Safety and efficacy of ZIIHERA have not been established in pediatric patients.
- **Geriatric Use**. Of the 80 patients who received ZIIHERA for unresectable or metastatic HER2-positive BTC, there were 39 (49%) patients 65 years of age and older. Thirty-seven (46%) were aged 65-74 years old and 2 (3%) were aged 75 years or older. No overall differences in safety or efficacy were observed between these patients and younger adult patients.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated November 21, 2024
104	Cover Page Interactive Data File (embedded as Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ZYMEWORKS INC.
(Registrant)

Date: November 21, 2024

By: */s/ Kenneth Galbraith*
Name: Kenneth Galbraith
Title: Chair, President and Chief Executive Officer

FDA Grants U.S. Approval of Ziihera® (zanidatamab-hrii) for the Treatment of Adults with Previously Treated, Unresectable or Metastatic HER2-positive (IHC 3+) Biliary Tract Cancer (BTC)

- *Ziihera is the first and only dual HER2-targeted bispecific antibody approved for HER2-positive BTC in the U.S.*
- *Ziihera received accelerated approval based on results including a 52% objective response rate and median duration of response of 14.9 months as determined by independent central review (ICR) from the HERIZON-BTC-01 clinical trial*
- *$25M milestone payment to be received from Jazz Pharmaceuticals in relation to the FDA approval; Zymeworks remains eligible for up to $500M in regulatory milestones*
- *Regulatory reviews of zanidatamab for BTC remain ongoing in China and Europe*
- *U.S. FDA approval of zanidatamab provides validation of the Company's proprietary Azymetric™ technology and capabilities for design and development of novel medicines*
- *Zanidatamab continues to be investigated in a number of additional tumor types, including Phase 3 trials in gastroesophageal adenocarcinomas (GEA) and metastatic breast cancer (mBC)*

Vancouver, British Columbia (November 21, 2024) – Zymeworks Inc. (Nasdaq: ZYME), a clinical-stage biotechnology company developing a diverse pipeline of novel, multifunctional biotherapeutics to improve the standard of care for difficult-to-treat diseases, today announced, with Jazz Pharmaceuticals, that the U.S. Food and Drug Administration (FDA) has granted accelerated approval of Ziihera® (zanidatamab-hrii) 50mg/mL for injection for intravenous use for the treatment of adults with previously-treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test.[1] *Ziihera* was approved under accelerated approval based on a 52% objective response rate (ORR) and a median duration of response (DOR) of 14.9 months as determined by independent central review (ICR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.[1] The approval of *Ziihera,* which previously received Breakthrough Therapy Designation from the FDA for this indication, is an important advance and offers the first and only dual HER2-targeted bispecific antibody and chemotherapy-free treatment for patients living with BTC.

---

1 ZIIHERA (zanidatamab-hrii) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

In late 2022, Zymeworks entered into a license and collaboration agreement with Jazz Pharmaceuticals Ireland Limited (a subsidiary of Jazz Pharmaceuticals plc, collectively referred to as Jazz), for the exclusive development and commercialization rights to zanidatamab across all indications in the United States, Europe, Japan and all other territories except for those Asia Pacific territories previously licensed by Zymeworks. This collaboration allowed the Company to leverage Jazz's global commercial infrastructure, together with BeiGene's complementary strengths in certain Asia Pacific countries, to enable the global, rapid advancement of zanidatamab in multiple tumor types with the potential to provide a foundational HER2-targeted therapy for patients with difficult-to-treat cancers and limited treatment options. Under the terms of the Jazz license and collaboration agreement, Zymeworks has earned a milestone payment of $25M based on the FDA approval in BTC. Zymeworks is also eligible to receive up to a further $500M in regulatory milestone payments and $862.5M in commercial milestone payments, as well as tiered royalties of 10% to 20% of net sales by Jazz.

This approval represents the first FDA-approved therapy in Zymeworks' pipeline, and validates the Company's novel Azymetric™ bispecific platform technology and internal research and development capabilities for novel multifunctional medicines.

"The FDA's accelerated approval of *Ziihera* marks the culmination of more than a decade of research and development at Zymeworks, highlighting our deep scientific expertise in multifunctional biotherapeutics and unwavering commitment to innovation in drug development," said Paul Moore, Ph.D., Chief Scientific Officer at Zymeworks. "This approval exemplifies our team's exceptional scientific capabilities to translate from an initial hypothesis for dual-HER2 blockade to a breakthrough treatment that offers new hope for patients with unresectable or metastatic HER2-positive BTC with limited treatment options and few approved therapies."

Through rigorous scientific investigation, innovative protein engineering, and proprietary Azymetric™ bispecific platform technology, Zymeworks developed the unique binding mechanism of zanidatamab-hrii, which enables it to bind to two extracellular sites on HER2. Binding of zanidatamab-hrii with HER2 results in internalization leading to a reduction of the receptor on the tumor cell surface. Zanidatamab-hrii induces complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). These mechanisms result in tumor growth inhibition and cell death in vitro and in vivo.

The FDA approval of *Ziihera* is based on compelling data from the HERIZON-BTC-01 trial, which included the evaluation of zanidatamab as a single agent in previously treated HER2-positive (as determined by Roche Diagnostic's PATHWAY® anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody companion diagnostic) BTC and is the largest Phase 2b clinical trial to date specifically for this patient population. The trial achieved its primary endpoint of confirmed objective response rate (cORR) by independent central review (ICR) and results were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting 2023, published in *The Lancet Oncology*, and included in the 2023 Best of ASCO® program. Longer follow-up data showing improvement upon previously reported DOR were reported at the ASCO Annual Meeting 2024.[1]

The Phase 3 HERIZON-BTC-302 confirmatory trial is ongoing to evaluate zanidatamab in combination with standard-of-care therapy versus standard-of-care therapy alone in the first-line setting for patients with HER2-positive BTC. Zanidatamab is also being investigated in a number of additional tumor types, including Phase 3 trials in gastroesophageal adenocarcinomas (GEAs) and metastatic breast cancer (mBC). The HERIZON-GEA-01 trial is evaluating the potential of zanidatamab plus chemotherapy with or without tislelizumab as first-line treatment for patients with advanced/metastatic HER2-positive GEAs and top-line progression-free survival data from this study is expected to be available in Q2-2025. The EmpowHER-303 trial is evaluating the potential of zanidatamab in combination with physician's choice chemotherapy for the treatment of HER2-positive mBC for patients who have progressed on, or are intolerant to, previous trastuzumab deruxtecan treatment.

"Our strategic collaboration with Jazz provided the optimal 'partner of choice' to continue the rapid advancement of zanidatamab, and we are extremely encouraged with Jazz's continued investment in and dedication to the development and commercialization of this novel therapy within their geographic territories," said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. "The combination of our strong balance sheet and anticipated revenue stream associated with zanidatamab positions us to accelerate the development of our wholly-owned R&D programs, while maintaining our projected cash runway into the second half of 2027."

Zymeworks continues to advance a diverse pipeline of novel therapeutics targeting difficult-to-treat cancers and other serious diseases, with several product candidates in various stages of development. The Company's in-house research and development capabilities, which were instrumental in zanidatamab's success, remain focused on delivering the next generation of innovative treatments. Zymeworks will host an in-person and virtual R&D day in New York on December 12, 2024, which will feature updates on the Company's portfolio of solid tumor targeting antibody-drug conjugates and T cell engager molecules, including preclinical progress supporting potential investigational new drug applications for multiple new product candidates in 2025, 2026 and beyond, and strategy and rationale for potential expansion into new therapeutic areas in hematological cancers and autoimmune and inflammatory diseases.

More information about *Ziihera*, the Full Prescribing Information, including Boxed Warning and Patient Information, is available here.

About Ziihera® (zanidatamab-hrii)

Ziihera (zanidatamab-hrii) is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Binding of zanidatamab-hrii with HER2 results in internalization leading to a reduction of the receptor on the tumor cell surface. Zanidatamab-hrii induces complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). These mechanisms result in tumor growth inhibition and cell death in vitro and in vivo.[1] In the United States, *Ziihera* is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test.[1] The U.S. Food and Drug Administration (FDA) granted accelerated approval for this indication based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).[1]

Zanidatamab is not approved anywhere else in the world.

Zanidatamab is being developed in multiple clinical trials as a targeted treatment option for patients with solid tumors that express HER2. Zanidatamab is being developed by Jazz and BeiGene, Ltd. (BeiGene) under license agreements from Zymeworks, which first developed the molecule.

The FDA granted Breakthrough Therapy designation for zanidatamab development in patients with previously treated HER2 gene-amplified BTC, and two Fast Track designations for zanidatamab: one as a single agent for refractory BTC and one in combination with standard-of-care chemotherapy for 1L gastroesophageal adenocarcinoma (GEA). Additionally, zanidatamab has received Orphan Drug designations from FDA for the treatment of BTC and GEA, as well as Orphan Drug designation from the European Medicines Agency for the treatment of BTC and gastric cancer.

More information about *Ziihera*, the Full Prescribing Information, including Boxed Warning and Patient Information, is available here.

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY
Exposure to ZIIHERA during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

ZIIHERA can cause fetal harm when administered to a pregnant woman. In literature reports, use of a HER2-directed antibody during pregnancy resulted in cases of oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death.

Verify the pregnancy status of females of reproductive potential prior to the initiation of ZIIHERA. Advise pregnant women and females of reproductive potential that exposure to ZIIHERA during pregnancy or within 4 months prior to conception can result in fetal harm. Advise females of reproductive potential to use effective contraception during treatment with ZIIHERA and for 4 months following the last dose of ZIIHERA.

Left Ventricular Dysfunction

ZIIHERA can cause decreases in left ventricular ejection fraction (LVEF). LVEF declined by >10% and decreased to <50% in 4.3% of 233 patients. Left ventricular dysfunction (LVD) leading to permanent discontinuation of ZIIHERA was reported in 0.9% of patients. The median

time to first occurrence of LVD was 5.6 months (range: 1.6 to 18.7). LVD resolved in 70% of patients.

Assess LVEF prior to initiation of ZIIHERA and at regular intervals during treatment. Withhold dose or permanently discontinue ZIIHERA based on severity of adverse reactions.

The safety of ZIIHERA has not been established in patients with a baseline ejection fraction that is below 50%.

Infusion-Related Reactions

ZIIHERA can cause infusion-related reactions (IRRs). An IRR was reported in 31% of 233 patients treated with ZIIHERA as a single agent in clinical studies, including Grade 3 (0.4%), and Grade 2 (25%). IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.4% of patients. IRRs occurred on the first day of dosing in 28% of patients; 97% of IRRs resolved within one day.

Prior to each dose of ZIIHERA, administer premedications to prevent potential IRRs. Monitor patients for signs and symptoms of IRR during ZIIHERA administration and as clinically indicated after completion of infusion. Have medications and emergency equipment to treat IRRs available for immediate use.

If an IRR occurs, slow, or stop the infusion, and administer appropriate medical management. Monitor patients until complete resolution of signs and symptoms before resuming. Permanently discontinue ZIIHERA in patients with recurrent severe or life-threatening IRRs.

Diarrhea

ZIIHERA can cause severe diarrhea.

Diarrhea was reported in 48% of 233 patients treated in clinical studies, including Grade 3 (6%) and Grade 2 (17%). If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Withhold or permanently discontinue ZIIHERA based on severity.

ADVERSE REACTIONS

Serious adverse reactions occurred in 53% of 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA. Serious adverse reactions in >2% of patients included biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhea (3.8%), gastric obstruction (3.8%), and fatigue (2.5%). A fatal adverse reaction of hepatic failure occurred in one patient who received ZIIHERA.
The most common adverse reactions in 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA (≥20%) were diarrhea (50%), infusion-related reaction (35%), abdominal pain (29%), and fatigue (24%).

USE IN SPECIFIC POPULATIONS

Pediatric Use

Safety and efficacy of ZIIHERA have not been established in pediatric patients.

Geriatric Use

Of the 80 patients who received ZIIHERA for unresectable or metastatic HER2-positive BTC, there were 39 (49%) patients 65 years of age and older. Thirty-seven (46%) were aged 65-74 years old and 2 (3%) were aged 75 years or older.

No overall differences in safety or efficacy were observed between these patients and younger adult patients.

About Biliary Tract Cancer

BTC, including gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, account for <1% of all adult cancers globally and are often associated with a poor prognosis.[2,3] The human epidermal growth factor receptor 2 (HER2) is a well-validated target for antitumor therapy in other cancers. Across the U.S., Europe, and Japan, approximately 12,000 people are diagnosed with HER2+ BTC annually.[4,5,6,7]

About Azymetric™

Azymetric™ is a heterodimeric antibody technology that gives the ability to engineer, screen, and effectively choose the optimal geometry and valency for our targeted treatments. These customized therapeutic antibodies are engineered to simultaneously bind to multiple distinct locations on a target or to multiple targets, resulting in unique mechanisms of action not accessible through typical monospecific antibodies. Azymetric™ antibodies can block multiple signaling pathways, recruit immune cells to tumors, enhance receptor clustering and internalization, and increase tumor-specific targeting. Zymeworks' other technologies can combine with Azymetric™ to engineer the antibody backbone of a bispecific antibody-drug conjugate or the base of a multispecific therapeutic, to overcome known therapeutic barriers and help design potential best-in-class bi-specifics and trispecifics.

About Zymeworks Inc.

Zymeworks is a global clinical-stage biotechnology company committed to the discovery, development, and commercialization of novel, multifunctional biotherapeutics. Zymeworks' mission is to make a meaningful difference in the lives of people impacted by difficult-to-treat cancers and other diseases. The Company's complementary therapeutic platforms and fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated antibody-based therapeutic candidates. Zymeworks

2 Valle JW, et al. Lancet 2021; 397:428-44

3 Siegel RL, et al. CA Cancer J Clin 2022; 72;7-33

4 BTC overall diagnosed patients as per SEER 22

5 Assumes anatomic subsites intrahepatic CCA, extrahepatic CCA, gallbladder cancer, and BTC unspecified

6 Assumes HER2 positivity rates per anatomical subsite from: Galdy, S., Lamarca, A., McNamara, M.G. et al. Cancer Metastasis Rev 36, 141–157 (2017), Nobuyoshi Hiraoka, et al. Human Pathology, Volume 105, 2020, Pages 9-19

7 Major markets: U.K, France, Germany, Spain, Italy. Note: HER2+ BTC patients in Jazz-controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd

engineered and developed zanidatamab, a HER2-targeted bispecific antibody using the Company's proprietary Azymetric™ technology. Zymeworks has entered into separate agreements with BeiGene, Ltd. (BeiGene) and Jazz Pharmaceuticals Ireland Limited (Jazz), granting each exclusive rights to develop and commercialize zanidatamab in different territories. Zanidatamab is currently being evaluated in multiple global clinical trials as a potential best-in-class treatment for patients with HER2-expressing cancers. The U.S. FDA granted accelerated approval of Ziihera® (zanidatamab-hrii) 50mg/mL for injection for intravenous use for the treatment of adults with previously-treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC). *Ziihera* is the first and only dual HER2-targeted bispecific antibody approved for HER2-positive BTC in the U.S. A BLA has also been accepted for review by the Center for Drug Evaluation (CDE) of the National Medical Products Administration (NMPA) in China. Zymeworks is rapidly advancing a robust pipeline of wholly-owned product candidates, leveraging its expertise in both antibody-drug conjugates and multispecific antibody therapeutics targeting novel pathways in areas of significant unmet medical need. Phase 1 studies for ZW171 and ZW191 are now actively recruiting with investigational new drug applications for ZW220 and ZW251 planned for 2025. In addition to Zymeworks' pipeline, its therapeutic platforms have been further leveraged through strategic partnerships with global biopharmaceutical companies. For information about Zymeworks, visit www.zymeworks.com and follow @ZymeworksInc on X.

Forward Looking Statements

This press release includes "forward-looking statements" or information within the meaning of the applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this press release include, but are not limited to, statements that relate to the conduct of an ongoing HERIZON-BTC-302 Phase 3 confirmatory trial to evaluate the efficacy and safety of zanidatamab and support global registration; ongoing clinical studies and regulatory reviews; the anticipated benefits of the collaboration agreements with Jazz and BeiGene, including Zymeworks' ability to receive any future milestone payments and royalties thereunder; the potential addressable market of zanidatamab; the timing of and results of interactions with regulators; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; the timing and status of ongoing and future studies and the related data; expectations regarding future regulatory filings and approvals and the timing thereof; potential safety profile and therapeutic effects of zanidatamab and Zymeworks' other product candidates; the commercial potential of technology platforms and product candidates; Zymeworks' ability to satisfy potential regulatory and commercial milestones with existing and future partners; anticipated continued receipt of revenue from existing and future partners; anticipated sufficiency of existing cash resources and certain anticipated revenues from zanidatamab to fund Zymeworks' planned operations into the second half of 2027; Zymeworks' ability to execute new collaborations and partnerships and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "anticipate", "potential", "will", "continues", and similar expressions are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans,

projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon Zymeworks' current expectations and various assumptions. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation: any of Zymeworks' or its partners' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; Zymeworks may not achieve milestones or receive additional payments under its collaborations; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; the impact of pandemics and other health crises on Zymeworks' business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks' behalf; zanidatamab may not be successfully commercialized; clinical trials and any future clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; Zymeworks' assumptions and estimates regarding its financial condition, future financial performance and estimated cash runway may be incorrect; and Zymeworks may be unable to maintain or enter into new partnerships or strategic collaborations.

Although Zymeworks believes that such forward-looking statements are reasonable, there can be no assurance they will prove to be correct. Investors should not place undue reliance on forward-looking statements. The above assumptions, risks and uncertainties are not exhaustive. Forward-looking statements are made as of the date hereof and, except as may be required by law, Zymeworks undertakes no obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances, or to reflect the occurrences of unanticipated events.

Contacts:

Investor Inquiries:

Shrinal Inamdar
Director, Investor Relations
(604) 678-1388
ir@zymeworks.com

Media Inquiries:

Diana Papove
Senior Director, Corporate Communications
(604) 678-1388

media@zymeworks.com